WEST

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Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Term	Documents
(2 NOT 3).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1
(L2 NOT L3).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	1

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L4

Refine Search | Recall Text | Clear

Search History

DATE: Wednesday, December 18, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L4	L2 not L3	1	L4
L3	L2 and (cancer or tumor or tumour)	16	L3
L2	(HSV-?) same (35.4 or R3616)	17	L2
L1	Brown-susanne-M$.in.	11	L1

END OF SEARCH HISTORY

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### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.11.17D

Last logoff:  14dec02 10:17:57
Logon file001 18dec02 13:06:28
           *** ANNOUNCEMENT ***
                     ***
--File 515 D&B Dun's Electronic Business Directory is now online
completely updated and redesigned. For details, see HELP NEWS 515.
                     ***
--File 990 - NewsRoom now contains May 2002 to present records.
File 993 - NewsRoom archive contains 2002 records from January 2002-
April 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002.
                     ***
--Alerts have been enhanced to allow a single Alert profile to be
stored and run against multiple files. Duplicate removal is available
across files and for up to 12 months. The Alert may be run according
to the file's update frequency or according to a custom
calendar-based schedule. There are no additional prices for these
enhanced features. See HELP ALERT for more information.
                     ***
--U.S. Patents Fulltext (File 654) has been redesigned with
new search and display features.  See HELP NEWS 654 for
information.
                     ***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
                     ***
--CLAIMS/US Patents (Files 340,341, 942) have been enhanced
with both application and grant publication level in a
single record. See HELP NEWS 340 for information.
                     ***
--SourceOne patents are now delivered to your email inbox
as PDF replacing TIFF delivery. See HELP SOURCE1 for more
information.
                     ***
--Important news for public and academic
libraries.  See HELP LIBRARY for more information.
                     ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                     ***
For information about the access to file 43 please see Help News43.
***
NEW FILES RELEASED
***Dialog NewsRoom - Current 3-4 months (File 990)
***Dialog NewsRoom - 2002 Archive (File 993)
***Dialog NewsRoom - 2001 Archive (File 994)
***Dialog NewsRoom - 2000 Archive (File 995)
***TRADEMARKSCAN-Finland (File 679)
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***TRADEMARKSCAN-Norway (File 678)
***TRADEMARKSCAN-Sweden (File 675)
***

UPDATING RESUMED
***Delphes European Business (File 481)
***

RELOADED
***D&B Dun's Electronic Business Directory (File 515)
***U.S. Patents Fulltext 1976-current (File 654)
***Population Demographics (File 581)
***Kompass Western Europe (File 590)
***D&B - Dun's Market Identifiers (File 516)

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CSA Files:
***Abstracts in New Technologies and Engineering (File 238)
***Aerospace Database (File 108)
***Aluminium Industry Abstracts (File 33)
***Applied Social Sciences Index and Abstracts (File 232)
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***Conference Papers Index (File 77)
***Engineered Materials Abstracts (File 293)
***ISMEC: Mechanical Engineering Abstracts (File 14)
***Life Sciences Collection (File 76)
***Linguistics and Language Behavior Abstracts (File 36)
***LISA (Library & Information Science Abstracts) (File 61)
***Materials Business File (File 269)
***METADEX: Metals Science (File 32)
***Oceanic Abstracts (File 28)
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***Water Resources Abstracts (File 117)
Other files:
***Chicago Tribune (File 632)
***Fort Lauderdale Sun Sentinel (File 497)
***The Orlando Sentinel (File 705)
***Newport News Daily Press (File 747)
***U.S. Patents Fulltext 1980-1989 (File 653)
***Washington Post (File 146)
***Books in Print (File 470)
***Court Filings (File 793)
***Publishers, Distributors & Wholesalers of the U.S. (File 450)
***State Tax Today (File 791)
***Tax Notes Today (File 790)
***Worldwide Tax Daily (File 792)

New document supplier
IMED has been changed to INFOTRIE (see HELP OINFOTRI)

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
****
KWIC is set to 50.
HILIGHT set on as '*'
* ** **

File 1:ERIC 1966-2002/Dec 13
(c) format only 2002 The Dialog Corporation

Set	Items	Description

Cost is in DialUnits
?b 155, 159, 5, 73

```
     18dec02 13:06:41 U[redacted]259876 Session D446.1
          $0.35    0.099 DialUnits File1
     $0.35  Estimated cost File1
     $0.04  TELNET
     $0.39  Estimated cost this search
     $0.39  Estimated total session cost   0.099 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Nov W3
*File 155: For updating information please see Help News155. Alert
feature enhanced with customized scheduling. See HELP ALERT.
  File 159:Cancerlit  1975-2002/Oct
         (c) format only 2002 Dialog Corporation
  File   5:Biosis Previews(R)  1969-2002/Dec W3
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Dec W2
         (c) 2002 Elsevier Science B.V.
*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
?s (HSV-?) (s) (35.4 or R3616)
             700  HSV-?
               0  35.4
              71  R3616
      S1       0  (HSV-?) (S) (35.4 OR R3616)
?s (HSV) (s) (mutant?)
           39287  HSV
          576061  MUTANT?
      S2    4306  (HSV) (S) (MUTANT?)
?s s2 (s) (35.4 or R3616)
            4306  S2
               0  35.4
              71  R3616
      S3      40  S2 (S) (35.4 OR R3616)
?s s3 and (tumor or cancer or tumour or neoplastic)
              40  S3
         2074819  TUMOR
         2194133  CANCER
          265750  TUMOUR
          561665  NEOPLASTIC
      S4      33  S3 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
?rd
...completed examining records
      S5      11  RD (unique items)
?t s5/3,k/all

 5/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13692094   22207923   PMID: 12219034
  Ionizing radiation potentiates the antitumor efficacy of oncolytic herpes
simplex virus G207 by upregulating ribonucleotide reductase.
  Stanziale  Stephen  F;  Petrowsky Henrik; Joe John K; Roberts Gretchen D;
Zager Jonathan S; Gusani Niraj J; Ben-Porat Leah; Gonen Mithat; Fong Yuman
  Hepatobiliary  Division,  Department of Surgery, Memorial Sloan-Kettering
Cancer Center, New York, NY 10021, USA.
  Surgery (United States)   Aug 2002,  132  (2)  p353-9,  ISSN 0039-6060
Journal Code: 0417347
  Contract/Grant  No.:  R01  CA72632;  CA;  NCI;  R01  CA75416;  CA;  NCI;
R01CA61524; CA; NCI
  Document type: Journal Article
```

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND: Replication-competent herpes simplex virus-1 (*HSV*-1) *mutants* have an oncolytic effect on human and animal cancers. The aim of this study was to determine whether G207, an *HSV*-1 *mutant*, can be combined with ionizing radiation (IR) to increase antitumor activity while decreasing treatment-associated toxicity. METHODS: This study was performed by using G207, a replication-competent *HSV*-1 *mutant* deficient in viral ribonucleotide reductase (RR) and the gamma(1)34.5 neurovirulence protein. The antitumor activity of G207 or IR was tested against HCT-8 human colorectal *cancer* cells in vitro and in an in vivo mouse subcutaneous *tumor* model. RESULTS: We demonstrated that G207 has significant oncolytic effect on HCT-8 cells in vitro in a cytotoxicity assay and in vivo in a mouse flank *tumor* model and that these effects are improved with low-dose IR. We further illustrated that the increased tumoricidal effect is dependent on the up-regulation...

... RR by IR measured by a functional bioassay for RR activity. Chemical inhibition of RR by hydroxyurea abrogates the enhanced effect. In contrast to G207, *R3616* , the parent virus of G207 that expresses functional RR, does not exhibit enhanced oncolysis when combined with IR. CONCLUSIONS: These data encourage clinical investigation of combination radiation therapy and *HSV* oncolytic therapy.

...; 1, Human--genetics--GE; Hydroxyurea--pharmacology--PD; Lac Operon; Mice; Proteins--genetics--GE; Radiation, Ionizing; Ribonucleotide Reductases--antagonists and inhibitors--AI; Ribonucleotide Reductases --genetics--GE; *Tumor* Cells, Cultured--cytology--CY; *Tumor* Cells, Cultured--virology--VI; Up-Regulation--radiation effects--RE; Viral Proteins--genetics--GE; Virus Replication--radiation effects--RE

5/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11326080 21376505 PMID: 11483960

Oncogenes in Ras signalling pathway dictate host-cell permissiveness to herpes simplex virus 1.

Farassati F; Yang A D; Lee P W
Cancer Biology Research Group, and Department of Microbiology and Infectious Diseases, University of Calgary Health Sciences Center, Calgary, Alberta T2N 4N1, Canada.

Nature cell biology (England) Aug 2001, 3 (8) p745-50, ISSN 1465-7392 Journal Code: 100890575
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The importance of herpes simplex viruses (*HSV*) as human pathogens and the emerging prospect of using *mutant* derivatives of *HSV*-1 as potential anti-*cancer* therapeutics have necessitated a thorough investigation into the molecular basis of host-cell permissiveness to *HSV*. Here we show that NIH-3T3 cells transformed with the oncogenes v-erbB, activated sos or activated ras become significantly more permissive to *HSV*-1. Inhibitors of the Ras signalling pathway, such as farnesyl transferase inhibitor 1 and PD98059, effectively suppressed *HSV*-1 infection of ras-transformed cells. Enhanced permissiveness of the transformed cells was linked to the inhibition of virus-induced activation (phosphorylation) of the double-stranded RNA-activated protein kinase (PKR), thereby allowing viral transcripts to be translated in these cells. An *HSV*-1-derived oncolytic *mutant*, *R3616*, was also found to infect preferentially both transformed cells and PKR-/- (but not PKR+/+) mouse embryo fibroblasts. These observations suggest that *HSV* -1 specifically targets cells with an activated Ras signalling pathway, and have important ramifications in the

use of engineered *HSV* *cancer* therapy, the development of strategies against *HSV* infections, and the controversial role of *HSV* in human cancers.

5/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11241558 21267426 PMID: 11353831
Oncolytic herpes simplex virus vector with enhanced MHC class I presentation and *tumor* cell killing.
Todo T; Martuza R L; Rabkin S D; Johnson P A
Molecular Neurosurgery Laboratory, Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA. todo@helix.mgh.harvard.edu
Proceedings of the National Academy of Sciences of the United States of America (United States) May 22 2001, 98 (11) p6396-401, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: NS32677; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Oncolytic herpes simplex virus vector with enhanced MHC class I presentation and *tumor* cell killing.
Oncolytic herpes simplex virus type 1 (*HSV*-1) vectors are promising therapeutic agents for *cancer*. Their efficacy depends on the extent of both intratumoral viral replication and induction of a host antitumor immune response. To enhance these properties while employing ample safeguards, two conditionally replicating *HSV*-1 vectors, termed G47Delta and R47Delta, have been constructed by deleting the alpha47 gene and the promoter region of US11 from gamma34.5-deficient *HSV*-1 vectors, G207 and *R3616* , respectively. Because the alpha47 gene product is responsible for inhibiting the transporter associated with antigen presentation (TAP), its absence led to increased MHC class I...

... deletion also places the late US11 gene under control of the immediate-early alpha47 promoter, which suppresses the reduced growth properties of gamma34.5-deficient *mutants*. G47Delta and R47Delta showed enhanced viral growth in a variety of cell lines, leading to higher virus yields and enhanced cytopathic effect in *tumor* cells. G47Delta was significantly more efficacious in vivo than its parent G207 at inhibiting *tumor* growth in both immune-competent and immune-deficient animal models. Yet, when inoculated into the brains of *HSV*-1-sensitive A/J mice at 2 x 10(6) plaque forming units, G47Delta was as safe as G207. These results suggest that G47Delta may...
...; Early Proteins--genetics--GE; Mice; Mice, Inbred BALB C; Mice, Nude; Neoplasm Transplantation; Neuroblastoma--immunology--IM; RNA-Binding Proteins--genetics--GE; T-Lymphocytes--immunology--IM; *Tumor* Cells, Cultured; Vero Cells; Viral Proteins--genetics--GE; Virus Replication

5/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10879477 20410789 PMID: 10955822
Oncolytic herpes simplex virus-1 lacking ICP34.5 induces p53-independent death and is efficacious against chemotherapy-resistant ovarian *cancer*.
Coukos G; Makrigiannakis A; Kang E H; Rubin S C; Albelda S M; Molnar-Kimber K L
Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia 19104, USA. gcoukos@obgyn.upenn.edu
Clinical cancer research : an official journal of the American Association for Cancer Research (UNITED STATES) Aug 2000, 6 (8)

p3342-53, ISSN 1078-04[illegible] Journal Code: 9502500
Contract/Grant No.: PO-CA66726-SI; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Oncolytic herpes simplex virus-1 lacking ICP34.5 induces p53-independent death and is efficacious against chemotherapy-resistant ovarian *cancer*.

Replication-restricted herpes simplex virus-1 (*HSV*-1) strains lacking ICP34.5 are emerging as powerful anticancer agents against several solid tumors including epithelial ovarian *cancer* (EOC). Although chemotherapy-resistant tumors would be likely candidates for treatment with *HSV*-1 *mutants* lacking ICP34.5, the efficacy of these *mutants* on such tumors is unknown. In the present study, we investigated whether chemotherapy resistance affects the response of ovarian *cancer* cells to *HSV*-*R3616*, an ICP34.5-deficient, replication-restricted *HSV* -1. Primary EOC cultures obtained from patients who varied in their responses to platinum/paclitaxel induction chemotherapy displayed similar sensitivity to *HSV*-*R3616*. Similarly, chemotherapy-sensitive ovarian *cancer* cells A2780 and PA-1, possessing wild-type p53, and their respective chemotherapy-resistant clones A2780/200CP, lacking p53 function, and PA-1/E6, permanently expressing the HPV E6 gene, were equally sensitive to *HSV* oncolysis. Because wild-type *HSV* can kill cells by apoptosis and nonapoptotic mechanisms, we investigated the involvement of apoptosis and the role of the p53 *tumor* suppressor gene in oncolysis induced by *HSV*-*R3616*. Infection of ovarian *cancer* cell lines by *HSV*-*R3616* was followed by cell death via apoptosis or nonapoptotic mechanisms as noted by morphology, cell cycle analysis, and in situ TUNEL assay. p53 protein levels remained unchanged, and Bax protein levels decreased in cells possessing intact p53 and that mainly underwent *HSV*-induced apoptosis. Loss of p53 function did not affect the frequency or rate of apoptosis or the sensitivity of EOC cells to the oncolytic effect of *HSV*-*R3616*. These results suggest that recombinant *HSV*-1 lacking ICP34.5 is capable of killing ovarian *cancer* cells that lack p53 function, resist apoptosis, and/or are chemotherapy resistant. These data support the hypothesis that *HSV* -based oncolytic therapy may be efficacious in chemotherapy-resistant tumors, including tumors that are deficient in p53.

...; Herpesvirus 1, Human--metabolism--ME; Ovarian Neoplasms--pathology --PA; Ovarian Neoplasms--virology--VI; Paclitaxel--pharmacology--PD; Protein p53--metabolism--ME; Proto-Oncogene Proteins--metabolism--ME; *Tumor* Cells, Cultured; Viral Proteins--genetics--GE; Virus Replication

5/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09724301 98144579 PMID: 9483585

Marker gene transfer and oncolysis of human Y79 retinoblastoma cells mediated by herpes simplex virus mutants.

Nicolo M; Chiocca E A
University Eye Clinic, Genoa, Italy.
Ophthalmic research (SWITZERLAND) 1998, 30 (1) p30-6, ISSN 0030-3747 Journal Code: 0267442
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Three different herpes simplex virus (*HSV*) *mutants*, designated hrR3, MGH-1 and *R3616* , were used to infect Y79 retinoblastoma cells grown in suspension. Two parameters were assayed: (a) vector-mediated gene expression, measured by histochemical staining of a transferred LacZ transgene, and (b) virus-mediated oncolysis, determined by the inability of infected cells to exclude trypan blue dye. The tested *HSV* *mutants* were found to infect cells grown in suspension at a relatively low multiplicity

of infection (MOI = 0.01) and were capable of transferring the LacZ gene as early as 2 days after infection. Furthermore, differences in oncolytic activity were observed amongst the tested viruses: MGH-1 and *R3616* exhibited 50% cell kill at a MOI of 0.1 over a period of 6 days, whereas hrR3-mediated oncolysis appeared less efficient. These studies...
...; Herpesvirus 1, Human--physiology--PH; Indoles--metabolism--ME; Plasmids--genetics--GE; Retinal Neoplasms--metabolism--ME; Retinal Neoplasms--pathology--PA; Retinoblastoma--metabolism--ME; Retinoblastoma --pathology--PA; *Tumor* Cells, Cultured

5/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09667351 98075065 PMID: 9414254
Therapeutic efficiency and safety of a second-generation replication-conditional HSV1 vector for brain *tumor* gene therapy.
Kramm C M; Chase M; Herrlinger U; Jacobs A; Pechan P A; Rainov N G; Sena-Esteves M; Aghi M; Barnett F H; Chiocca E A; Breakefield X O
Molecular Neurogenetics Unit, Massachusetts General Hospital, Charlestown 02129, USA.
Human gene therapy (UNITED STATES) Nov 20 1997, 8 (17) p2057-68, ISSN 1043-0342 Journal Code: 9008950
Contract/Grant No.: CA69246; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Therapeutic efficiency and safety of a second-generation replication-conditional HSV1 vector for brain *tumor* gene therapy.
A second-generation replication-conditional herpes simplex virus type 1 (*HSV*) vector defective for both ribonucleotide reductase (RR) and the neurovirulence factor gamma34.5 was generated and tested for therapeutic safety and efficiency in two different experimental brain *tumor* models. In culture, cytotoxic activity of this double *mutant* *HSV* vector, MGH-1, for 9L gliosarcoma cells was similar to that of the *HSV* *mutant*, *R3616* , which is defective only for gamma34.5, but was significantly weaker than that of the *HSV* *mutant* hrR3, which is defective only for RR. The diminished tumoricidal effect of the gamma34.5 *mutants* could be accounted for by their reduced ability to replicate in 9L cells. The MGH-1 vector did not achieve significant prolongation of survival in vivo in the syngeneic 9L rat gliosarcoma model for either single brain *tumor* focus or multiple intracerebral and leptomeningeal tumors, when the vector was applied intratumorally or intrathecally, respectively, and with or without subsequent ganciclovir (GCV) treatment. In identical 9L brain *tumor* models with single and multiple foci, application of hrR3 with or without GCV was previously shown to result in marked long-term survival. Contrary to the findings with intrathecal injection of hrR3, no vector-related mortality was observed in any animals treated with MGH-1. Thus, in these rat brain *tumor* models, the double *mutant*, replication-conditional *HSV* vector MGH-1 showed a higher therapeutic safety than the RR-minus vector, hrR3, but had clearly decreased therapeutic efficiency compared to hrR3. The development of new *HSV* vectors for brain *tumor* gene therapy will require a balance between maximizing therapeutic efficacy and minimizing toxicity to the brain. Standardized application in brain *tumor* models as presented here will help to screen new *HSV* vectors for these requirements.
...; Ganciclovir--therapeutic use--TU; Gene Deletion; Genetic Vectors --toxicity--TO; Gliosarcoma--secondary--SC; Meningeal Neoplasms--secondary --SC; Rats; Rats, Inbred F344; Ribonucleotide Reductases--metabolism--ME; *Tumor* Cells, Cultured; Vero Cells; Viral Proteins--metabolism--ME; Virus Replication

5/3,K/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE

09357880 97249519 PMID: 9095405

A novel multiply-mutated HSV-1 strain for the treatment of human brain tumors.

Pyles R B; Warnick R E; Chalk C L; Szanti B E; Parysek L M

Department of Cell Biology, University of Cincinnati, OH 45267, USA.

Human gene therapy (UNITED STATES) Mar 20 1997, 8 (5) p533-44, ISSN 1043-0342 Journal Code: 9008950

Contract/Grant No.: NS31145; NS; NINDS; T32-CA59268; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A promising approach for the therapeutic treatment of brain tumors utilizes replication-competent, neuroattenuated herpes simplex virus-1 (*HSV*-1) *mutants*. This approach requires mutation of *HSV*-1 to eliminate killing of normal, nondividing cells of the brain (e.g., neurons). We have generated a *HSV*-1 double-*mutant*, designated 3616UB, by interrupting the uracil DNA glycosylase (UNG) gene in a previously studied ICP34.5 *mutant*, *R3616*. The *HSV*-1-encoded UNG gene is required for efficient *HSV*-1 replication in nondividing cells, but is dispensable for replication in rapidly dividing cells. The specific function of the *HSV*-1 ICP34.5 gene is not completely clear, but it is thought to be necessary for viral replication in cells of the nervous system, because...

... are fully neuroattenuated. Strain 3616UB did not replicate in primary neuronal cultures in vitro or in mouse brain, but efficiently killed six of six human *tumor* cell lines within 6 days in vitro and successfully infected and replicated within brain *tumor* xenografts. The potential safety of 3616UB for human use is enhanced by an unexpected hypersensitivity to the antiherpetic drug ganciclovir. These data suggest that 3616UB...

... brain tumors. Intratumoral injection of 3616UB into human medulloblastoma or angiosarcoma xenografts established in severe combined immunodeficient (SCID) mice produced significant growth arrest and some *tumor* regressions. Strain 3616UB was as effective as *R3616* in this therapy study and did not cause any obvious distress in the treated animals. Together, the data show that 3616UB is a very safe alternative to other *HSV*-1 *mutants* because the presence of two mutations reduces the possibility of recombinational events in situ that could lead to the generation of virulent viral progeny during...

...; Genetic Vectors--drug effects--DE; In Situ Hybridization, Fluorescence; Lac Operon--genetics--GE; Mice; Mice, SCID; Mutation; Rats; Simplexvirus--drug effects--DE; Simplexvirus--physiology--PH; *Tumor* Cells, Cultured; Vero Cells

5/3,K/8 (Item 8 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

09348617 97262038 PMID: 9108452

Evaluation of genetically engineered herpes simplex viruses as oncolytic agents for human malignant brain tumors.

Andreansky S; Soroceanu L; Flotte E R; Chou J; Markert J M; Gillespie G Y ; Roizman B; Whitley R J

Department of Surgery, University of Alabama at Birmingham School of Medicine, 35294-0006, USA.

Cancer research (UNITED STATES) Apr 15 1997, 57 (8) p1502-9, ISSN 0008-5472 Journal Code: 2984705R

Contract/Grant No.: AI-24009; AI; NIAID; P20-NS31096; NS; NINDS; T35-HL07473; HL; NHLBI; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: N
Record type: Completed

Earlier studies have shown that genetically engineered herpes simplex viruses (e.g., *HSV*-1) are effective in killing malignant *tumor* cells both in vitro and in various murine *tumor* models. This report focuses on a panel of five genetically engineered viral *mutants* of the gamma(1)34.5 gene, which was shown previously to cause reduction in viral replication and associated neurovirulence of *HSV*. These include *R3616*, which has both copies of gamma(1)34.5 deleted, R4009, which has a stop codon inserted after codon 28 in both copies of the...

... a stop codon precluding the translation of the COOH-terminal domain of the gamma(1)34.5 gene. We report the following: (a) all five *mutant* HSVs were avirulent in experimental animals but were cytotoxic for human *tumor* cells in vitro and in vivo; (b) the gamma(1)34.5- *HSV* replicated in human glioma cells almost as efficiently as wild-type *HSV*-1(F) based on replication assays, in situ hybridization for viral DNA, and expression of infected cell protein 27; (c) capacity of *mutant* HSVs to kill human cells derived from glioblastoma multiforme (CH-235MG, D-37MG, D-54MG, D-65MG, U-251MG, U-373MG, and SK-MG-1...

... Hs-683), anaplastic glioma (U-87MG and U-138MG), gliosarcoma (D-32GS), or normal human astrocytes demonstrated that glioma cells varied in their susceptibility to *HSV*-mediated cytotoxicity and that cultured astrocytes were two to three orders of magnitude less susceptible to killing than were malignant glia; and (d) scid mice...

... were coinoculated at the time of intracranial transplantation with 106 U251MG or D-54MG human glioma cells or received the cells intratumorally 5 days after *tumor* induction and experienced significant increases in median survivals, with no histopathological indication of an infectious encephalitic process. Genetically engineered gamma(1)34.5- *HSV* *mutants* appear to be a potentially safe biotherapeutic agent for experimental treatment of uniformly fatal malignant brain tumors.

5/3,K/9 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

02411198 PMID: 97616181
Cytotoxicity of a novel recombinant herpes viral vector (Meeting abstract).
Carroll; Chiocca; Tanabe
Dept of Surgery and Neurosurgery Service, Massachusetts General Hospital, Boston, MA
Proc Annu Meet Am Assoc Cancer Res 1997, 38, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Entry of wild type herpes simplex virus (*HSV*) into *tumor* cells leads to viral replication followed by cytolysis, and accordingly, construction of *HSV* *mutants* that replicate selectively in tumors may be an effective strategy against *cancer*. We have previously demonstrated that one such *mutant* , hrR3, replicates in diffuse colon carcinoma liver metastases but not in surrounding normal liver hrR3 is defective in ribonucleotide reductase expression and its replication is limited to mitotically active cells Nonetheless, the potential neurovirulence of hrR3 remains a theoretical concern for *HSV* treatment of tumors. In the present study we have examined the cytotoxicity of 2 engineered *HSV* vectors:(i) *R3616* (a neurovirulence gene *mutant*); and (ii) MGH1 (mutated ribonucleotide reductase and neurovirulence genes) HT29 human colon carcinoma cells were infected with hrR3, *R3616* , and MGH1 using several multiplicities of

infection (MOI) and c survival was quantitated [redacted] days later hrR3 destroyed 70% of the cells at an MOI of 001 In comparison, *R3616* and MGH1 required an MOI of 10 for comparable cytotoxicity Neurovirulence gene mutation markedly attenuated *HSV* cytotoxicity in colorectal carcinoma Such dramatic attenuation may render *R3616* and MGH1 ineffective agents for colon *cancer* therapy.

5/3,K/10 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

02231740 PMID: 96606660
Use of genetically engineered HSV-1 viruses in treatment of malignant intracerebral gliomas (Meeting abstract).
Soroceanu; Chatterjee; Chambers; Andreansky; Chou; Whitley; Roizman; Gillespie
University of Alabama at Birmingham, Birmingham, AL 35294
FASEB J 1995, 9 (3), ISSN 0892-6638
Document Type: JOURNAL ARTICLE
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

We examined the oncolytic properties of recombinant herpes simplex virus-1 (*HSV* -1) on glioma cells, both in vitro and in vivo to examine their potential for experimental therapy of malignant brain tumors (gliomas). Three genetically altered *HSV* *mutants* , retaining the thymidine kinase gene, were investigated: *R3616* (deletion in the neurovirulence gene gamma1 34.5), R4009 (stop codon inserted in gamma1 34.5) and R849 (R4009 variant containing a Lac Z insert...

... blot analyses and immunohistochemistry confirmed that all three viruses replicated in, and caused cytolysis of, glioma cell lines of both murine and human origin. Both *R3616* and R4009 exhibited oncolytic potential in vivo in a dose dependent fashion against mouse glioma cells (MT539 MG) by significantly prolonging the survival of scid (CB1.7) mice bearing intracerebral tumors. R4009 was more effective in killing glioma cells in vitro and in extending *tumor* -bearer survival. Neither virus produced neurotoxicity at doses up to 2.5 x 10(6) pfu. Pretreatment of mice with Ganciclovir (50 mg/kg x 7 days) partially reversed the *mutant* *HSV* protective effect. Our data demonstrates direct antitumor effects of genetically engineered *HSV* *mutants* and supports their potential use as novel therapy of gliomas in humans.

5/3,K/11 (Item 3 from file: 159)
DIALOG(R)File 159:Cancerlit

02228568 PMID: 96601947
Brain *tumor* therapy using mutated, replication-competent herpes simplex virus (Meeting abstract).
Rabkin; Mineta; Miyatake; Yazaki; Martuza
Department of Neurosurgery, Georgetown University Medical Center, Washington, DC 20007
Proc Annu Meet Am Assoc Cancer Res 1995, 36, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Brain *tumor* therapy using mutated, replication-competent herpes simplex virus (Meeting abstract).
We have demonstrated that genetically engineered *mutants* of herpes simplex virus (*HSV*) have therapeutic potential for malignant brain

tumors. Our strategy is to maximize *tumor*-cell killing while minimizing alteration and death of surrounding normal brain cells. In order to create a safe and effective vector we have characterized *HSV* mutations that affect neurovirulence and viral replication in nondividing cells. *R3616*, deletion of the gamma 34.5 gene, is not neurovirulent yet still able to destroy human glioblastoma cells in vitro and in vivo. HrR3, insertion...

... to destroy glioblastoma cells. A new vector, containing mutations in both gamma 34.5 and ICP6, has been constructed. It is able to destroy brain *tumor* cells in vitro and in vivo and is safe when injected intracerebrally into *HSV*-sensitive nonhuman primates. This *mutant* is also hypersensitive to anti-*HSV* drugs (ganciclovir) and the replicating virus can be detected in *tumor* sections with X-gal histochemistry. These studies suggest that replication-competent *HSV* vectors should be considered for human therapy.
?ds

```
Set     Items   Description
S1          0   (HSV-?) (S) (35.4 OR R3616)
S2       4306   (HSV) (S) (MUTANT?)
S3         40   S2 (S) (35.4 OR R3616)
S4         33   S3 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
S5         11   RD (unique items)
?s s5 and (1716)
             11  S5
            517  1716
      S6     0  S5 AND (1716)
?s (herpes (w) simplex (w) virus) (s) (1716)
         127379  HERPES
         100642  SIMPLEX
        1270197  VIRUS
            517  1716
      S7    79  (HERPES (W) SIMPLEX (W) VIRUS) (S) (1716)
?s s7 and (tumor or cancer or tumour or neoplastic)
             79  S7
        2074819  TUMOR
        2194133  CANCER
         265750  TUMOUR
         561665  NEOPLASTIC
      S8    51  S7 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
?rd s8
...examined 50 records  (50)
...completed examining records
      S9    21  RD S8 (unique items)
?s s9 and (mesothlioma or ovarian or melanoma or (bladder (w) cancer))
             21  S9
              8  MESOTHLIOMA
         249918  OVARIAN
         190154  MELANOMA
         257657  BLADDER
        2194133  CANCER
          45267  BLADDER(W)CANCER
     S10     6  S9 AND (MESOTHLIOMA OR OVARIAN OR MELANOMA OR (BLADDER
                (W) CANCER))
?t s10/3,k/all
```

10/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11112483 21121343 PMID: 11229673
Intralesional injection of *herpes* *simplex* *virus* *1716* in metastatic *melanoma*.
MacKie R M; Stewart B; Brown S M
Lancet (England) Feb 17 2001, 357 (9255) p525-6, ISSN 0140-6736
Journal Code: 2985213R
Document type: Clinical Trial; Letter

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Intralesional injection of *herpes* *simplex* *virus* *1716* in metastatic *melanoma*.

We have previously shown that avirulent but replication-competent *herpes* *simplex* *virus* (HSV) *1716* causes cell death in human *melanoma* cell lines in vitro and selectively replicates in *melanoma* tissue in nude mice. We now present a pilot study of intratumoral injection of HSV1716 into subcutaneous nodules of metastatic *melanoma* in five patients with stage 4 *melanoma*. Two patients each received one injection, two received two injections, and one received four injections of 10(3) plaque-forming units HSV1716. In one patient, flattening of previously palpable *tumour* nodules was seen 21 days after two direct injections of HSV1716, and in injected nodules from all three patients who received two or more injections there was microscopic evidence of *tumour* necrosis. Immunohistochemical staining of injected nodules revealed evidence of virus replication confined to *tumour* cells. These findings suggest that HSV1716 is non-toxic and could be of therapeutic benefit in patients with metastatic *melanoma*.

Descriptors: Biological Therapy; **Melanoma*--therapy--TH; *Simplexvirus --physiology--PH; *Melanoma*--secondary--SC; Pilot Projects; Simplexvirus --genetics--GE; Viral Proteins--genetics--GE; Virus Replication

10/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10950660 20511572 PMID: 11059765

Role of the immune response during neuro-attenuated herpes simplex virus-mediated *tumor* destruction in a murine intracranial *melanoma* model.

Miller C G; Fraser N W
Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia 19104-6076, USA.

Cancer research (UNITED STATES) Oct 15 2000, 60 (20) p5714-22, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: CA77903; CA; NCI; NS39546; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Role of the immune response during neuro-attenuated herpes simplex virus-mediated *tumor* destruction in a murine intracranial *melanoma* model.

Neuro-attenuated *herpes* *simplex* *virus*-1 (HSV-1) gamma34.5 mutants can slow progression of preformed tumors and lead to complete regression of some tumors. However, the role of the immune response in this process is poorly understood. Syngenic DBA/2 *tumor*-bearing mice treated with HSV-1 *1716* fourteen days after *tumor* implantation had significant prolongation in survival when compared with mice treated with viral growth sera (mock; 38.9 +/- 2.3 versus 24.9 +/- 0.6...

... treated on day 7 had complete regression of the tumors. However, no difference was observed in the mean survival rates of viral- or mock-treated *tumor* -bearing SCID mice (15 +/- 1.7 versus 14.8 +/- 2.2, respectively). When DBA/2 mice syngenic for the *tumor* were depleted of leukocytes by cyclophosphamide administration (before and during viral administration), there was again no significant difference observed in the survival times (19.0 +/- 1.9 versus 19.5 +/- 2.7, respectively). These data demonstrate that the immune response contributes to the viral-mediated *tumor* destruction and the increase in survival. Immune cell infiltration was up-regulated, specifically CD4+ T cells and macrophages (which are found early after viral administration...

Descriptors: Brain Neoplasms--immunology--IM; *Brain Neoplasms--therapy --TH; *Herpesvirus 1, Human--physiology--PH; **Melanoma*, Experimental --immunology--IM; **Melanoma*, Experimental--therapy--TH; Apoptosis --physiology--PH; Brain Neoplasms--virology--VI; CD4-Positive T-Lymphocytes --immunology--IM; CD8-Positive T-Lymphocytes--immunology--IM; *Cancer* Vaccines--administration and dosage--AD; *Cancer* Vaccines--immunology --IM; Herpes Simplex Virus Vaccines--administration and dosage--AD; Herpes Simplex Virus Vaccines--immunology--IM; Herpesvirus 1, Human--genetics--GE; Herpesvirus 1, Human--immunology--IM; Injections, Intraventricular; Killer Cells, Natural--immunology--IM; Macrophages--immunology--IM; *Melanoma*, Experimental--virology--VI; Mice; Mice, Inbred DBA; Mice, SCID; Neoplasm Transplantation; Vaccines, Attenuated--administration and dosage--AD; Vaccines, Attenuated--immunology--IM

Chemical Name: *Cancer* Vaccines; Herpes Simplex Virus Vaccines; Vaccines, Attenuated

10/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10513460 20049750 PMID: 10585055

Oncolytic therapy using a mutant type-1 herpes simplex virus and the role of the immune system.

Lambright E S; Caparrelli D J; Abbas A E; Toyoizumi T; Coukos G; Molnar-Kimber K L; Kaiser L R

Harrison Department of Surgical Research, University of Pennsylvania Medical Center, Philadelphia, USA.

Annals of thoracic surgery (UNITED STATES) Nov 1999, 68 (5) p1756-60; discussion 1761-2, ISSN 0003-4975 Journal Code: 15030100R

Contract/Grant No.: PO-66726-S1; PHS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: *Herpes* *simplex* *virus* (HSV)-*1716* , a replication-restricted *herpes* *simplex* *virus* type 1, has shown efficacy as an oncolytic treatment for central nervous system tumors, breast *cancer*, *ovarian* *cancer* , and malignant mesothelioma. We evaluated the efficacy of HSV-*1716* in a murine lung *cancer* model, Lewis lung carcinoma. METHODS: Lewis lung carcinoma cells were infected with HSV-*1716* and implanted in the flanks of mice at varying ratios of infected to uninfected cells. *Tumor* burden was assessed by measurement of the weight of the *tumor* nodule. The role of the immune system was examined by performing experiments in both immunocompetent and SCID mice. Tumors were implanted in the opposite flank to evaluate the vaccine effect. RESULTS: In immunocompetent and SCID animals, ratio of 1:10 (infected-to-uninfected) cells completely prevented *tumor* formation and ratio of 1:100 suppressed *tumor* growth. Established tumors at a distant site in the groups receiving HSV-*1716* infected cells showed no difference in size versus control, suggesting absence of a vaccine effect. CONCLUSIONS: We conclude that HSV-*1716* may provide a oncolytic therapy for lung *cancer* even in the absence of immune system induction and a "carrier" cell could potentially deliver this vector.

Descriptors: Carcinoma, Lewis Lung--immunology--IM; *Herpesvirus 1, Human --immunology--IM; **Tumor* Lysis Syndrome--immunology--IM; *Viruses --immunology--IM; Carcinoma, Lewis Lung--virology--VI; Disease Models, Animal; Gene Therapy; Herpesvirus 1, Human--genetics--GE; Mice; Mice, Inbred C57BL; Mice, SCID; Neoplasm Transplantation; *Tumor* Lysis Syndrome --virology--VI; Viruses--genetics--GE

10/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10328623 99316804 PMID: 10389942

Use of carrier cells to deliver a replication-select herpes simplex virus-1 mutant for the intraperitoneal therapy of epithelial *ovarian* *cancer*.

Coukos G; Makrigiannakis A; Kang E H; Caparelli D; Benjamin I; Kaiser L R ; Rubin S C; Albelda S M; Molnar-Kimber K L

Department of Obstetrics and Gynecology, University of Pennsylvania Medical Center, Philadelphia 19104, USA.

Clinical cancer research : an official journal of the American Association for Cancer Research (UNITED STATES) Jun 1999, 5 (6) p1523-37, ISSN 1078-0432 Journal Code: 9502500

Contract/Grant No.: PO-66726-S1; PHS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Use of carrier cells to deliver a replication-selective herpes simplex virus-1 mutant for the intraperitoneal therapy of epithelial *ovarian* *cancer*.

Epithelial *ovarian* *cancer* (EOC) remains localized within the peritoneal cavity in a large number of patients, lending itself to i.p. approaches of therapy. In the present study, we investigated the effect of replication-selective *herpes* *simplex* *virus* -1 (HSV-1) used as an oncolytic agent against EOC and the use of human teratocarcinoma PA-1 as carrier cells for i.p. therapy. HSV-*1716* , a replication-competent attenuated strain lacking ICP34.5, caused a direct dose-dependent oncolytic effect on EOC cells in vitro. A single i.p. administration of 5 x 10(6) plaque-forming units resulted in a significant reduction of *tumor* volume and *tumor* spread and an increase in survival in a mouse xenograft model. PA-1 cells supported HSV replication in vitro and bound preferentially to human *ovarian* carcinoma surfaces compared with mesothelial surfaces in vitro and in vivo. In comparison with the administration of HSV-*1716* alone, irradiated PA-1 cells, infected at two multiplicities of infection with HSV-*1716* and injected i.p. at 5 x 10(6) cells/animal, led to a significant *tumor* reduction in the two models tested and the significant prolongation of mean survival in one model. Histological evaluation revealed extensive necrosis in *tumor* areas infected by HSV-*1716*. Immunohistochemistry against HSV-1 revealed areas of viral infection within *tumor* nodules, which persisted for several weeks after treatment. Administration of HSV-infected PA-1 carrier cells resulted in larger areas of *tumor* infected by the virus. Our results indicate that replication-competent attenuated HSV-1 exerts a potent oncolytic effect on EOC, which may be further enhanced...

... the utilization of a delivery system with carrier cells, based on amplification of the viral load and possibly on preferential binding of carrier cells to *tumor* surfaces.

Descriptors: Neoplasms, Glandular and Epithelial--therapy--TH; **Ovarian* Neoplasms--therapy--TH; *Simplexvirus--genetics--GE; *Teratocarcinoma --virology--VI...; Transplantation; Neoplasms, Glandular and Epithelial --metabolism--ME; Neoplasms, Glandular and Epithelial--mortality--MO; Neoplasms, Glandular and Epithelial--pathology--PA; Neoplasms, Glandular and Epithelial--virology--VI; *Ovarian* Neoplasms--metabolism--ME; *Ovarian* Neoplasms--mortality--MO; *Ovarian* Neoplasms--pathology--PA; *Ovarian* Neoplasms--virology--VI; Survival Rate; Teratocarcinoma --pathology--PA; *Tumor* Cells, Cultured; Virus Replication

10/3,K/5 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

11956226 BIOSIS NO.: 199900202335

Immune response during neuro-attenuated HSV-1 1716 treatment of murine intracranial melanomas.

AUTHOR: Miller C G; Fraser N W

AUTHOR ADDRESS: Dep. Mi[redacted]biology, Univ. Pa., Philadelph PA 19104**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 40p659 March, 1999
CONFERENCE/MEETING: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999
SPONSOR: American Association for Cancer Research
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

DESCRIPTORS:
...MAJOR CONCEPTS: *Tumor* Biology
...ORGANISMS: HSV-1 {*herpes* *simplex* *virus*-1} (Herpesviridae...

...anti-*tumor* effect, neuro-attenuated, mutant *1716*
DISEASES: intracranial *melanoma*--*neoplastic* disease, nervous system disease
METHODS & EQUIPMENT: brain *tumor* therapy...

10/3,K/6 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10357648 BIOSIS NO.: 199698812566
Replication-restricted herpes simplex virus-based treatment of localized non-CNS malignancy.
AUTHOR: Kucharczuk J; Randazzo B; Elshami A; Sterman D; Rizk N; Brown M; Molnar-Kimber K; Litzky L; Fraser N; Kaiser L; Albelda S
AUTHOR ADDRESS: Thoracic Oncol. Lab, Univ. Penna. Med. Cent., Philadelphia, PA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 37 (0):p342 1996
CONFERENCE/MEETING: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

MISCELLANEOUS TERMS: *BLADDER* *CANCER*; ...

...BRAIN *CANCER*; ...

...*HERPES* *SIMPLEX* *VIRUS* TYPE *1716* MUTANT...
...*OVARIAN* CARCINOMA
?ds

Set	Items	Description
S1	0	(HSV-?) (S) (35.4 OR R3616)
S2	4306	(HSV) (S) (MUTANT?)
S3	40	S2 (S) (35.4 OR R3616)
S4	33	S3 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
S5	11	RD (unique items)
S6	0	S5 AND (1716)
S7	79	(HERPES (W) SIMPLEX (W) VIRUS) (S) (1716)
S8	51	S7 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
S9	21	RD S8 (unique items)
S10	6	S9 AND (MESOTHLIOMA OR OVARIAN OR MELANOMA OR (BLADDER (W) CANCER))

```
?s s9 not s10
              21  S9
               6  S10
     S11      15  S9 NOT S10
?s s11 not s5
              15  S11
              11  S5
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S12 15 S11 NO 5
?t s12/3,k/all

12/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10926671 20476827 PMID: 11020355
Effect of preexisting anti-herpes immunity on the efficacy of herpes simplex viral therapy in a murine intraperitoneal *tumor* model.
Lambright E S; Kang E H; Force S; Lanuti M; Caparrelli D; Kaiser L R; Albelda S M; Molnar-Kimber K L
Thoracic Oncology Research Laboratory, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania 19104, USA.
Molecular therapy : the journal of the American Society of Gene Therapy (UNITED STATES) Oct 2000, 2 (4) p387-93, ISSN 1525-0016
Journal Code: 100890581
Contract/Grant No.: P50-CA-83638; CA; NCI; PO1-CA66726; CA; NCI; RO1-74958; PHS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Effect of preexisting anti-herpes immunity on the efficacy of herpes simplex viral therapy in a murine intraperitoneal *tumor* model.
HSV-*1716*, a replicating nonneurovirulent *herpes* *simplex* *virus* type 1, has shown efficacy in treating multiple types of human tumors in immunodeficient mice. Since the majority of the human population has been previously exposed to *herpes* *simplex* *virus*, the efficacy of HSV-based oncolytic therapy was investigated in an immunocompetent animal *tumor* model. EJ-6-2-Bam-6a, a *tumor* cell line derived from h-ras-transformed murine fibroblast, exhibit a diffuse growth pattern in the peritoneal cavity of BALB/c mice and replicate HSV-*1716* to titers observed in human tumors. An established intraperitoneal (ip) *tumor* model of EJ-6-2-Bam-6a in naive and HSV-immunized mice was used to evaluate the efficacy of single or multiple ip administrations of HSV-*1716* (4 x 10(6) pfu/treatment) or of carrier cells, which are irradiated, ex vivo virally infected EJ-6-2-Bam-6a cells that can...

... treated, HSV-naive animals. Prior immunization of the mice with HSV did not significantly decrease the median survival of the single or multiply treated HSV-*1716* or the carrier cell-treated groups. These studies support the development of replication-selective herpes virus mutants for use in localized intraperitoneal malignancies.

12/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10759979 20302347 PMID: 10845724
Toxicity evaluation of replication-competent *herpes* *simplex* *virus* (ICP 34.5 null mutant *1716*) in patients with recurrent malignant glioma.
Rampling R; Cruickshank G; Papanastassiou V; Nicoll J; Hadley D; Brennan D; Petty R; MacLean A; Harland J; McKie E; Mabbs R; Brown M
Beatson Oncology Centre, Western Infirmary, Glasgow, UK.
Gene therapy (ENGLAND) May 2000, 7 (10) p859-66, ISSN 0969-7128
Journal Code: 9421525
Comment in Gene Ther. 2000 May;7(10) 815-6; Comment in PMID 10845717
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Toxicity evaluation of replication-competent *herpes* *simplex* *virus* (ICP 34.5 null mutant *1716*) in patients with recurrent malignant glioma.
The *herpes* *simplex* *virus* (HSV) ICP34.5 null mutant *1716*

replicates selectively actively dividing cells and ha een proposed as a potential treatment for *cancer*, particularly brain tumours. We present a clinical study to evaluate the safety of *1716* in patients with relapsed malignant glioma. Following intratumoural inoculation of doses up to 10(5) p.f.u., there was no induction of encephalitis, no adverse clinical symptoms, and no reactivation of latent HSV. Of nine patients treated, four are currently alive and well 14-24 months after *1716* administration. This study demonstrates the feasibility of using replication-competent HSV in human therapy.

12/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10531791 20075752 PMID: 10609661

Combined therapy with chemotherapeutic agents and *herpes* *simplex* *virus* type 1 ICP34.5 mutant (HSV-*1716*) in human non-small cell lung *cancer*.

Toyoizumi T; Mick R; Abbas A E; Kang E H; Kaiser L R; Molnar-Kimber K L

Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.

Human gene therapy (UNITED STATES) Dec 10 1999, 10 (18) p3013-29, ISSN 1043-0342 Journal Code: 9008950

Contract/Grant No.: CA16520-24; CA; NCI; CA66727-S1; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Combined therapy with chemotherapeutic agents and *herpes* *simplex* *virus* type 1 ICP34.5 mutant (HSV-*1716*) in human non-small cell lung *cancer*.

A replication-selective *herpes* *simplex* *virus* type 1 ICP34.5 mutant (HSV-*1716*) has shown efficacy both in vitro and in vivo against human non-small cell lung *cancer* (NSCLC) cell lines but complete eradication of *tumor* has not been accomplished with a single viral treatment in our murine xenograft models. Therefore, strategies to enhance the efficacy of this treatment were investigated. We determined the oncolytic activity of HSV-*1716* in NCI-H460 cells in combination with each of four chemotherapeutic agents: mitomycin C (MMC), cis-platinum II (cis-DDP), methotrexate (MTX), or doxorubicin (ADR). Isobologram analysis was performed to evaluate the interaction between the viral and chemotherapeutic agents. The oncolytic effect of HSV-*1716* in combination with MMC was synergistic in two of five NSCLC cell lines. In the other three cell lines, the combined effect appeared additive. No...

... observed. The in vivo effect of this combination was then examined in a murine xenograft model. NCI-H460 flank tumors were directly injected with HSV-*1716* (4 x 106 PFU) followed by intravenous MMC administration (0.17 mg/kg) 24 hr later. After 3 weeks, the mean *tumor* weight in the combined treatment group was significantly less than either individual treatment in an additive manner. The synergistic dose of MMC neither augmented nor inhibited viral replication in vitro and HSV-*1716* infection did not upregulate DT-diaphorase, which is the primary enzyme responsible for MMC activation. In summary, the combination of HSV-*1716* with common chemotherapeutic agents may augment the effect of HSV-based therapy in the treatment of NSCLC.

...; drug therapy--DT; Lung Neoplasms--pathology--PA; Methotrexate --therapeutic use--TU; Mice; Mice, SCID; Mitomycin--therapeutic use--TU; NAD(P)H Dehydrogenase (Quinone)--metabolism--ME; *Tumor* Cells, Cultured

12/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10054194 99038608 PMID: 9821167

Histopathological responses in the CNS following inoculation with a non-neurovirulent mutant (*1716*) of *herpes* *simplex* *virus* type 1 (HSV 1): relevance for gene and *cancer* therapy.

McKie E A; Brown S M; MacLean A R; Graham D I
Glasgow University Neurovirology Research Laboratories, UK.

Neuropathology and applied neurobiology (ENGLAND) Oct 1998, 24 (5) p367-72, ISSN 0305-1846 Journal Code: 7609829
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Histopathological responses in the CNS following inoculation with a non-neurovirulent mutant (*1716*) of *herpes* *simplex* *virus* type 1 (HSV 1): relevance for gene and *cancer* therapy.

The RL1 gene of *herpes* *simplex* *virus* (HSV) encodes a polypeptide, ICP34.5 which is a specific virulence determinant. RL1 null mutants fail to replicate in both the PNS and CNS and...

... in actively dividing cells but fail to replicate in growth arrested or terminally differentiated cells. This selective replication phenotype has highlighted their use as both *tumour* killing agents and gene delivery vehicles particularly to the nervous system. Before their full potential can be assessed, however, it is necessary to determine the...

... induced following direct intracerebral inoculation. Fourteen mice were injected in the left cerebral hemisphere with a high dose of the HSV-1, RL1 null mutant *1716*. At regular time intervals up to 28 days, the mice were killed and the distribution of virus antigen, histopathological changes and immune responses in the...

...determined by H & E staining and immunohistochemistry. Control mice were injected with either wild type HSV-1 or buffer. At early times post-inoculation with *1716*, there is a low grade meningoencephalitis with a limited inflammatory response. This is accompanied by virus antigen expression confined to the site of inoculation. By...

12/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09747525 98178646 PMID: 9519831

A neuroattenuated ICP34.5-deficient herpes simplex virus type 1 replicates in ependymal cells of the murine central nervous system.

Kesari S; Lasner T M; Balsara K R; Randazzo B P; Lee V M; Trojanowski J Q ; Fraser N W
The Wistar Institute, Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.

Journal of general virology (ENGLAND) Mar 1998, 79 (Pt 3) p525-36, ISSN 0022-1317 Journal Code: 0077340
Contract/Grant No.: CA-36245; CA; NCI; MH10915; MH; NIMH; NS29390; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Herpes *simplex* *virus* type 1 (HSV-1) variant *1716* is deleted in the gene encoding ICP34.5 and is neuroattenuated after intracranial inoculation of mice. Although the mechanism of attenuation is unclear, this property has been exploited to eliminate experimental brain tumours. Previously, it was shown that infectious *1716* was recoverable for up to 3 days after intracranial inoculation suggesting that there may be limited replication in the central nervous system (CNS). Here it is demonstrated that *1716* replicates in specific cell types (predominantly CNS ependymal cells) of BALB/c mice, using immunohistochemical, immunofluorescence, in

situ hybridization and [redacted]us titration studies. While *1 *-infected mice exhibited no overt signs of encephalitis, histological analysis showed a persistent loss of the ependymal lining. Thus, although ICP34.5-deficient viruses are...

... murine CNS. A detailed understanding of the mechanism(s) of neuroattenuation and limited replication could lead to the rational design of safe HSV vectors for *cancer* and gene therapy in the CNS.

12/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09628934 98062157 PMID: 9400985
***Herpes* *simplex* *virus* *1716*, an ICP 34.5 null mutant, is unable to replicate in CV-1 cells due to a translational block that can be overcome by coinfection with SV40.**
Randazzo B P; Tal-Singer R; Zabolotny J M; Kesari S; Fraser N W
The Wistar Institute, Philadelphia, PA 19104, USA.
Journal of general virology (ENGLAND) Dec 1997, 78 (Pt 12) p3333-9, ISSN 0022-1317 Journal Code: 0077340
Contract/Grant No.: 1KO8CA65839; CA; NCI; NS33768; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

***Herpes* *simplex* *virus* *1716*, an ICP 34.5 null mutant, is unable to replicate in CV-1 cells due to a translational block that can be overcome by coinfection...**
Herpes *simplex* *virus* (HSV) mutants lacking the gene encoding infected cell protein (ICP) 34.5 exhibit an attenuated phenotype in models of pathogenesis and have been used for experimental *cancer* therapy. Recently it was shown that the HSV ICP 34.5 protein functions to prevent the host cell-induced double-stranded RNA-activated protein kinase (PKR)-dependent translational block that normally occurs during virus infection. We now report that an HSV ICP 34.5 mutant called HSV-*1716* is unable to replicate in the simian kidney cell-derived line CV-1, due to a translational block. Moreover, we find that this block can be overcome by simian virus 40 (SV40). This has been shown directly by infecting CV-1 cells with SV40 and HSV-*1716* simultaneously, and indirectly via HSV-*1716* infection of COS-1 cells (CV-1 cells transformed by an origin-defective mutant of SV40 that codes for wild-type T antigen). The translational...

12/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09018151 96388176 PMID: 8795577
Selective in vitro replication of herpes simplex virus type 1 (HSV-1) ICP34.5 null mutants in primary human CNS tumours--evaluation of a potentially effective clinical therapy.
McKie E A; MacLean A R; Lewis A D; Cruickshank G; Rampling R; Barnett S C ; Kennedy P G; Brown S M
Neurovirology Research Laboratories/Department of Neurology, Glasgow University, UK.
British journal of cancer (SCOTLAND) Sep 1996, 74 (5) p745-52, ISSN 0007-0920 Journal Code: 0370635
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Primary tumours of the central nervous system (CNS) are an important cause of *cancer* -related deaths in adults and children. CNS tumours are

mostly glial cell origin and are predominan astrocytomas. Conventional therapy of high-grade gliomas includes...

... adjuvant chemotherapy provides little improvement in survival time and hence assessment of novel therapies is imperative. We have evaluated the potential therapeutic use of the *herpes* *simplex* *virus* (HSV) mutant *1716* in the treatment of primary brain tumours. The mutant is deleted in the RL1 gene and fails to produce the virulence factor ICP34.5. *1716* replication was analysed in both established human glioma cell lines and in primary cell cultures derived from human *tumour* biopsy material. In the majority of cultures, virus replication occurred and consequential cell death resulted. In the minority of *tumour* cell lines which are non-permissive for mutant replication, premature shut-off of host cell protein synthesis was induced in response to lack of expression...

... ICP34.5. Hence RL1-negative mutants have the distinct advantage of providing a double hit phenomenon whereby cell death could occur by either pathway. Moreover, *1716* , by virtue of its ability to replicate selectively within a *tumour* cell, has the potential to deliver a 'suicide' gene product to the required site immediately. It is our opinion that HSV which fails to express ICP34.5 could provide an effective *tumour* therapy.

...; drug effects--DE; Herpesvirus 1, Human--isolation and purification --IP; Immediate-Early Proteins--biosynthesis--BI; Mutagenesis, Insertional; Nervous System Neoplasms--virology--VI; Proteins--biosynthesis--BI; *Tumor* Cells, Cultured

12/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08721625 96083561 PMID: 7474937

Therapy of experimental human brain tumors using a neuroattenuated herpes simplex virus mutant.

Kesari S; Randazzo B P; Valyi-Nagy T; Huang Q S; Brown S M; MacLean A R; Lee V M; Trojanowski J Q; Fraser N W

Wistar Institute, Philadelphia, Pennsylvania, USA.

Laboratory investigation; a journal of technical methods and pathology (UNITED STATES) Nov 1995, 73 (5) p636-48, ISSN 0023-6837
Journal Code: 0376617

Contract/Grant No.: MH10915-01; MH; NIMH; NS33768; NS; NINDS; T32-NS07180 ; NS; NINDS; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: Engineered *herpes* *simplex* *virus* (HSV) strains previously have been shown to offer a potential therapeutic alternative to conventional treatment modalities for brain tumors. Because HSV Type 1 strain *1716* has a deletion in the gamma 34.5 neurovirulence gene that renders it avirulent in the mouse central nervous system, we have assessed its potential to induce selective lysis of *tumor* cells versus neurons in vitro and in vivo. EXPERIMENTAL DESIGN: To do this, we studied parental HSV-1 strain 17+ and strain *1716* using human embryonal carcinoma cells (NT2 cells). These cells resemble neuronal progenitor cells and can be induced to differentiate into neurons (NT2N) with retinoic acid...

... mice resulted in lethal brain tumors, and grafts of NT2N cells resulted in the integration of NT2N cells. RESULTS: In vitro studies showed that strain *1716* replicates in and spreads on monolayers of NT2 cells but not in NT2N cells. In vivo, strain *1716* replicated preferentially in NT2 tumors as evidenced by immunohistochemical staining for viral antigens, by in situ hybridization for HSV-specific transcripts, and by titration of virus from brains with *tumor* after intracranial injection of the virus into these mice. The temporal regression of NT2 tumors in mice treated with

strain *1716* was dem[redacted]trated in vivo by magnetic onance imaging. Electron microscopy and studies of DNA fragmentation suggested that regression of NT2 brain tumors in strain *1716*-treated mice was mainly caused by a nonapoptotic, lytic mode of cell death. Finally, strain *1716* -treated NT2 *tumor* -bearing mice survived more than twice as long as mock-treated *tumor* -bearing mice, and these differences in survival (25 vs. 9 weeks) were statistically significant ($p < 0.03$). CONCLUSIONS: We conclude from these studies that strain *1716* induces regression of human neural tumors established in the brains of nude mice, resulting in their prolonged survival.
...; pathology--PA; Cell Death; Herpesvirus 1, Human--genetics--GE; Immunohistochemistry; Magnetic Resonance Imaging; Mice; Mice, Nude; Microscopy, Electron; Mutation; Neoplasm Transplantation; Survival Rate; Time Factors; *Tumor* Cells, Cultured; Virus Replication

12/3,K/9 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13881101 BIOSIS NO.: 200200509922
Phase 1 trial of herpes simplex virus, HSV1716 following injection into brain adjacent to *tumour* in patients with primary malignant glioma.
AUTHOR: Harrow S; Papanastassiou V; Brown S M; Fraser M; Rampling R(a)
AUTHOR ADDRESS: (a)University of Glasgow, Glasgow**UK
JOURNAL: British Journal of Cancer 86 (Supplement 1):pS26-S27 June, 2002
MEDIUM: print
CONFERENCE/MEETING: British Cancer Research Meeting 2002 Glasgow, UK June 30-July 03, 2002
ISSN: 0007-0920
RECORD TYPE: Citation
LANGUAGE: English

Phase 1 trial of herpes simplex virus, HSV1716 following injection into brain adjacent to *tumour* in patients with primary malignant glioma.
DESCRIPTORS:
ORGANISMS: *Herpes* *simplex* *virus* *1716* (Herpesviridae...
...DISEASES: *neoplastic* disease, nervous system disease, therapy

12/3,K/10 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13842723 BIOSIS NO.: 200200471544
HSV1716 persistence in primary human glioma cells in vitro.
AUTHOR: Harland J; Papanastassiou V; Brown S M(a)
AUTHOR ADDRESS: (a)Neurovirology Research Laboratories, Inst. of Neurological Sciences, Southern General Hospital, Glasgow, G51 4TF**UK
JOURNAL: Gene Therapy 9 (17):p1194-1198 September, 2002
MEDIUM: print
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: replication competent mutant of herpes simplex virus which is in trial in glioma patients. We have demonstrated that HSV1716 is non-toxic when delivered into *tumour* or into brain adjacent to *tumour* , yet replicates within *tumour* cells. *Tumour* tissue, from one patient treated 2.5 years previously with intra-tumoural HSV1716, was put into culture. The cultured cells were shown to be glial...

...the possibility that in tumours in vivo a similar phenomenon may take place. If this were the case, then HSV1716 has the potential to kill *tumour* cells over a prolonged period of time.

DESCRIPTORS:
...MAJOR CONCEPTS: *Tumor* Biology
ORGANISMS: *herpes* *simplex* *virus* *1716* (Herpesviridae...
...DISEASES: *neoplastic* disease, nervous system disease, therapy

12/3,K/11 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13632940 BIOSIS NO.: 200200261761
The potential for efficacy of the modified (ICP 34.5-) herpes simplex virus HSV1716 following intratumoural injection into human malignant glioma: A proof of principle study.
AUTHOR: Papanastassiou V(a); Rampling R; Fraser M; Petty R; Hadley D; Nicoll J; Harland J; Mabbs R; Brown M
AUTHOR ADDRESS: (a)Department of Neurosurgery, Institute of Neurological Sciences, Southern General Hospital, Glasgow, G51 4TF**UK
JOURNAL: Gene Therapy 9 (6):p398-406 March, 2002
MEDIUM: print
ISSN: 0969-7128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: demonstrating that the virus survives and replicates when injected into the tumours of patients. Since HSV replication is a cytolytic process it must result in *tumour* cell killing. Twelve patients with biopsy-verified HGG received an intratumoural injection of 105 plaque-forming units (p.f.u.) of HSV1716. Four to 9...
...input dose was recovered from the injection site. HSV DNA was detected by PCR at the sites of inoculation in 10 patients and at distal *tumour* sites in four. HSV-specific antigen was detected in *tumour* tissue from two patients. In five patients an immunological response to HSV1716, as detected by changes in levels of IgG and IgM, was demonstrated. This...
DESCRIPTORS:
ORGANISMS: *herpes* *simplex* *virus* {HSV} (Herpesviridae...

...*1716* mutant, gene vector, intratumoral injection, replication competent
...DISEASES: diagnosis, *neoplastic* disease, nervous system disease, therapy

12/3,K/12 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11889060 BIOSIS NO.: 199900135169
Combination therapy with *herpes* *simplex* *virus* type 1 ICP34.5 mutant (HSV-*1716*) and common chemotherapeutic agents for human non-small cell lung *cancer* (NSCLC).
AUTHOR: Toyoizumi Takane(a); Abbas Abbas E(a); Caparrelli David J(a); Kang Eugene H(a); Albelda Steven M; Kaiser Larry R(a); Molnar-Kimber Katherine L(a)
AUTHOR ADDRESS: (a)Dep. Surg., Univ. Pa. Sch. Med., Philadelphia, PA**USA
JOURNAL: Cancer Gene Therapy 5 (6 CONF. SUPPL.):pS7-S8 Nov.-Dec., 1998
CONFERENCE/MEETING: Seventh International Conference on Gene Therapy of Cancer San Diego, California, USA November 19-21, 1998
ISSN: 0929-1903
RECORD TYPE: Citation
LANGUAGE: English

Combination therapy with *herpes* *simplex* *virus* type 1 ICP34.5 mutant (HSV-*1716*) and common chemotherapeutic agents for human non-small cell lung *cancer* (NSCLC).

DESCRIPTORS:
...MAJOR CONCEPTS: *Tumor* Biology
...ORGANISMS: human non-small cell lung *cancer*

12/3,K/13 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10791185 BIOSIS NO.: 199799412330
Use of a "replication-restricted" herpes virus to treat experimental human malignant mesothelioma.
AUTHOR: Kucharczuk John C; Randazzo Bruce; Chang Michael Y; Amin Kunjlata M ; Elshami Ashraf A; Sterman Daniel H; Rizk Nabil P; Molnar-Kimber Katherine L; Brown S Moira; MacLean Alasdair R; Litzky Leslie A; Fraser Nigel W; Albelda Steven M; Kaiser Larry R
AUTHOR ADDRESS: Div. Thoracic Surgery, Univ. Pa. Med. Center, 4 Silverstein, 3400 Spruce St., Philadelphia, PA 19104**USA
JOURNAL: Cancer Research 57 (3):p466-471 1997
ISSN: 0008-5472
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: malignant mesothelioma cells supported the growth of HSV-1716 and were efficiently lysed in vitro. i.p. injection of HSV-1716 into animals with established *tumor* nodules reduced *tumor* burden and significantly prolonged survival in an animal model of non-central nervous system-localized human malignancy without dissemination or persistence after i.p. injection...
MISCELLANEOUS TERMS: ...*HERPES* *SIMPLEX* *VIRUS*-*1716*; ...

...*NEOPLASTIC* DISEASE...

...*TUMOR* BIOLOGY

12/3,K/14 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10782464 BIOSIS NO.: 199799403609
Treatment of retinoblastoma arising in transgenic mice with a HSV-1 deletion mutant virus.
AUTHOR: Martin M(a); Albert D M; Kennedy S; Brown M; Kenna P(a); Windle J J ; Brandt C; MacLean A R; Humphries P(a); Farrar G J(a)
AUTHOR ADDRESS: (a)Wellcome Ocular Genetics Unit, Dep. Genetics, Trinity Coll. Dublin, Dublin**Ireland
JOURNAL: Cancer Gene Therapy 3 (6 CONF. SUPPL.):pS21 1996
CONFERENCE/MEETING: Fifth International Conference on Gene Therapy of Cancer San Diego, California, USA November 14-16, 1996
ISSN: 0929-1903
RECORD TYPE: Citation
LANGUAGE: English

...MAJOR CONCEPTS: *Tumor* Biology
MISCELLANEOUS TERMS: ...*HERPES* *SIMPLEX* *VIRUS*-1-STRAIN-*1716*-3...

...*NEOPLASTIC* DISEASE...

...*TUMOR* BIOLOGY

12/3,K/15 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06613794 EMBASE No: 6278570

Selective in vitvo replication of herpes simplex virus type 1 (HSV-1) ICP34.5 null mutants in primary human CNS tumours- evaluation of a potentially effective clinical therapy

McKie E.A.; Maclean A.R.; Lewis A.D.; Cruickshank G.; Rampling R.; Barnett S.C.; Kennedy P.G.E.; Brown S.M.

Neurovirol Res Lab Dept Neurology, Glasgow Univ Inst Neurolog Sciences, Southern General Hospital, Govan Road,Glasgow G51 4TF United Kingdom

British Journal of Cancer (BR. J. CANCER) (United Kingdom) 1996, 74/5 (745-752)

CODEN: BJCAA ISSN: 0007-0920

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Primary rumours of the central nervous system (CNS) are an important cause of *cancer*-related deaths in adults and children. CNS tumours are mostly glial cell in origin and are predominantly astrocytomas. Conventional therapy of high-grade gliomas includes...

...adjuvant chemotherapy provides little improvement in survival rime and hence assessment of novel therapies is imperative. We have evaluated the potential therapeutic use of the *herpes* *simplex* *virus* (HSV) mutant *1716* in the treatment of primary brain tumours. The mutant is deleted in the RL1 gene and fails to produce the virulence factor ICP34.5. *1716* replication was analysed in both established human glioma cell lines and in primary cell cultures derived from human *tumour* biopsy material. In the majority of cultures, virus replication occurred and consequential cell death resulted. In the minority of *tumour* cell lines which are non-permissive for mutant replication, premature shut-off of host cell protein synthesis was induced in response to lack of expression...

...ICP34.5. Hence RL1-negative mutants have the distinct advantage of providing a double hit phenomenon whereby cell death could occur by either pathway. Moreover, *1716*, by virtue of its ability to replicate selectively within a *tumour* cell, has the potential to deliver a 'suicide' gene product to the required site immediately. It is our opinion that HSV which fails to express ICP34.5 could provide an effective *tumour* therapy.

MEDICAL DESCRIPTORS:

**cancer* therapy; *central nervous system *tumor*; *herpes simplex virus 1 adjuvant chemotherapy; article; astrocytoma; brain *tumor*; *cancer* cell culture; *cancer* mortality; *cancer* radiotherapy; *cancer* surgery; cell death; controlled study; gene deletion; glia cell; human; human cell; priority journal; protein expression; protein synthesis; target cell destruction; virus mutant; virus replication

SECTION HEADINGS:

004 Microbiology: Bacteriology, Mycology, Parasitology and Virology

016 *Cancer*

030 Clinical and Experimental Pharmacology

037 Drug Literature Index

?ds

Set	Items	Description
S1	0	(HSV-?) (S) (35.4 OR R3616)
S2	4306	(HSV) (S) (MUTANT?)
S3	40	S2 (S) (35.4 OR R3616)
S4	33	S3 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
S5	11	RD (unique items)
S6	0	S5 AND (1716)
S7	79	(HERPES (W) SIMPLEX (W) VIRUS) (S) (1716)
S8	51	S7 AND (TUMOR OR CANCER OR TUMOUR OR NEOPLASTIC)
S9	21	RD S8 (unique items)
S10	6	S9 AND (MESOTHLIOMA OR OVARIAN OR MELANOMA OR (BLADDER (W) CANCER))
S11	15	S9 NOT S10
S12	15	S11 NOT S5

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               $4.20  20 Type(s) in Format  3
            $4.20  20 Types
     $6.32  Estimated cost File155
            $1.57    0.534 DialUnits File159
               $0.78  3 Type(s) in Format  3
            $0.78  3 Types
     $2.35  Estimated cost File159
            $3.57    0.638 DialUnits File5
              $14.00  8 Type(s) in Format  3
           $14.00  8 Types
    $17.57  Estimated cost File5
            $8.82    0.980 DialUnits File73
               $2.50  1 Type(s) in Format  3
            $2.50  1 Types
    $11.32  Estimated cost File73
            OneSearch, 4 files,  2.815 DialUnits FileOS
     $1.73  TELNET
    $39.29  Estimated cost this search
    $39.68  Estimated total session cost   2.914 DialUnits


### Status: Signed Off. (8 minutes)
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